i-STAT CG4+ Cartridge

Intended for US only

NAME

i-STAT CG4+ Cartridge – REF 03P85-51

INTENDED USE

The i-STAT CG4+ cartridge with the i-STAT 1 System is intended for use in the *in vitro* quantification of pH, ***P***O_2, ***P***CO_2, and lactate in arterial or venous whole blood in point of care or clinical laboratory settings.

Analyte	Intended Use
pH	pH, ***P***O_2, and ***P***CO_2 measurements are used in the diagnosis, monitoring, and treatment of respiratory disturbances and metabolic and respiratory-based acid-base disturbances.
Partial pressure of oxygen (***P***O_2)	
Partial pressure of carbon dioxide (***P***CO_2)	
Lactate	Lactate measurements are used in (1) the diagnosis and treatment of lactic acidosis in conjunction with measurements of blood acid/base status, (2) monitoring tissue hypoxia and strenuous physical exertion, and (3) diagnosis of hyperlactatemia.

SUMMARY AND EXPLANATION / CLINICAL SIGNIFICANCE

Measured:

pH

pH is an index of the acidity or alkalinity of the blood with an arterial pH of <7.35 indicating an acidemia and >7.45 alkalemia [1].

Partial Pressure of Oxygen (***P***O_2)

PO_2 (partial pressure of oxygen) is a measurement of the tension or pressure of oxygen dissolved in blood. Some causes for decreased values of ***P***O_2 include decreased pulmonary ventilation (e.g., airway obstruction or trauma to the brain), impaired gas exchange between alveolar air and pulmonary capillary blood (e.g., bronchitis, emphysema, or pulmonary edema), and alteration in the flow of blood within the heart or lungs (e.g., congenital defects in the heart or shunting of venous blood into the arterial system without oxygenation in the lungs).

Partial Pressure of Carbon Dioxide (***P***CO_2)

PCO_2 along with pH is used to assess acid-base balance. ***P***CO_2 (partial pressure of carbon dioxide), the respiratory component of acid-base balance, is a measure of the tension or pressure of carbon dioxide dissolved in the blood. ***P***CO_2 represents the balance between cellular production of CO_2 and ventilatory removal of CO_2 and a change in ***P***CO_2 indicates an alteration in this balance. Causes of primary respiratory acidosis (increase in ***P***CO_2) are airway obstruction, sedatives and anesthetics, respiratory distress syndrome, and chronic obstructive pulmonary disease. Causes of primary respiratory alkalosis (decreased ***P***CO_2) are hypoxia (resulting in hyperventilation) due to chronic heart failure, edema and neurologic disorders, and mechanical hyperventilation.

Lactate (Lac)

Elevated levels of lactate are mainly found in conditions of hypoxia such as shock, hypovolemia, and left ventricular failure; in conditions associated with diseases such as diabetes mellitus, neoplasia, and liver disease; and in conditions associated with drugs or toxins such as ethanol, methanol, or salicylates.[2]

Hyperlactatemia is an indicator commonly used to detect tissue hypoperfusion, particularly in the case of sepsis [3 4 5], but also in trauma [6 7 8] and surgical [9 10 11] settings.

TEST PRINCIPLE

Measured:

pH

pH is measured by direct potentiometry. In the calculation of results for pH, concentration is related to potential through the Nernst equation.

PO_2

PO_2 is measured amperometrically. The oxygen sensor is similar to a conventional Clark electrode. Oxygen permeates through a gas permeable membrane from the blood sample into an internal electrolyte solution where it is reduced at the cathode. The oxygen reduction current is proportional to the dissolved oxygen concentration.

PCO_2

PCO_2 is measured by direct potentiometry. In the calculation of results for *P*CO_2, concentration is related to potential through the Nernst equation.

Lactate (Lac)

Lactate is measured amperometrically. The enzyme lactate oxidase, immobilized in the lactate biosensor, selectively converts lactate to pyruvate and hydrogen peroxide (H_2O_2). The liberated hydrogen peroxide is oxidized at a platinum electrode to produce a current which is proportional to the sample lactate concentration.

$$\text{L-Lactate} + O_2 \xrightarrow{\text{Lactate Oxidase}} \text{Pyruvate} + H_2O_2$$

$$H_2O_2 \xrightarrow{\text{Platinum electrode}} 2H^+ + O_2 + 2e^-$$

Temperature "Correction" Algorithm

pH, *P*O_2, and *P*CO_2 are temperature-dependent quantities and are measured at 37°C. The pH, *P*O_2, and *P*CO_2 readings at a body temperature other than 37°C can be 'corrected' by entering the patient's temperature on the chart page of the analyzer. In this case, blood gas results will be displayed at both 37°C and the patient's temperature.

pH, *P*O_2, and *P*CO_2 at the patient's temperature (T_p) are calculated as follows [12]:

$$pH(T_p) = pH - 0.0147(T_p - 37) + 0.0065(7.4 - pH)(T_p - 37)$$

$$PO_2(T_p) = PO_2 \times 10^{\frac{5.49\times10^{-11}\,PO_2^{3.88} + 0.071}{9.72\times10^{-9}\,PO_2^{3.88} + 2.30}(T_p - 37)}$$

$$PCO_2(T_p) = PCO_2 \times 10^{0.019(T_p - 37)}$$

Calculated:

HCO_3, TCO_2, and BE

- Bicarbonate (HCO_3) is the most abundant buffer in the blood plasma, is an indicator of the buffering capacity of blood. Regulated primarily by the kidneys, HCO_3 is the metabolic component of acid-base balance. Causes of primary metabolic acidosis (decrease calculated HCO_3) are

ketoacidosis, lactate acidosis (hypoxia), and diarrhea. Causes of primary metabolic alkalosis (increase calculated HCO_3) are vomiting and antacid treatment.

- Total carbon dioxide (TCO_2) is a measure of carbon dioxide which exists in several states: CO_2 in physical solution or loosely bound to proteins, bicarbonate (HCO_3) or carbonate (CO_3) anions, and carbonic acid (H_2CO_3). Measurement of TCO_2 as part of an electrolyte profile is useful chiefly to evaluate HCO_3 concentration. TCO_2 and HCO_3 are useful in the assessment of acid-base imbalance (along with pH and $\boldsymbol{P}CO_2$) and electrolyte imbalance.
    - The calculated TCO_2 provided by the i-STAT System is determined from the measured and reported values of pH and $\boldsymbol{P}CO_2$ according to a simplified and standardized form of the Henderson-Hasselbalch equation below. [12]
    - This calculated TCO_2 measurement is metrologically traceable to the i-STAT pH and $\boldsymbol{P}CO_2$ measurements, which are in turn traceable to primary standard reference materials for pH and $\boldsymbol{P}CO_2$. Like all calculated parameters reported by the i-STAT System, the user can independently determine TCO_2 values from the reported pH and $\boldsymbol{P}CO_2$ measurements using a combination of the equation for HCO_3 and the equation for TCO_2 below.
- Base excess (BE) of the extracellular fluid or standard base excess is defined as the concentration of titratable base minus the concentration of titratable acid when titrating the average ECF (plasma plus interstitial fluid) to an arterial plasma pH of 7.40 at $\boldsymbol{P}CO_2$ of 40 mmHg at 37 °C. Excess concentration of base in the average ECF remains virtually constant during acute changes in the $\boldsymbol{P}CO_2$ and reflects only non-respiratory component of pH-disturbances.

  When a cartridge includes sensors for both pH and $\boldsymbol{P}CO_2$, HCO_3, TCO_2, and BE are calculated. [12]

  $\log HCO_3 = pH + \log \boldsymbol{P}CO_2 - 7.608$
  $TCO_2 = HCO_3 + 0.03\boldsymbol{P}CO_2$
  $BE_{ecf} = HCO_3 - 24.8 + 16.2(pH - 7.4)$
  $BE_b = (1 - 0.014*Hb) * [\ HCO_3 - 24.8 + (1.43 * Hb + 7.7) * (pH - 7.4)\ ]$

sO_2

- Oxygen saturation (sO_2) is the amount of oxyhemoglobin expressed as a fraction of the total amount of hemoglobin able to bind oxygen (oxyhemoglobin plus deoxyhemoglobin).
- sO_2 is calculated from measured $\boldsymbol{P}O_2$ and pH and from HCO_3 calculated from measured $\boldsymbol{P}CO_2$ and pH. However, this calculation assumes normal affinity of oxygen for hemoglobin. It does not take into account erythrocyte diphosphoglycerate (2,3-DPG) concentrations which affect the oxygen dissociation curve. The calculation also does not take into account the effects of fetal hemoglobin or dysfunctional hemoglobins (carboxy-, met-, and sulfhemoglobin). Clinically significant errors can result from incorporation of such an estimated sO_2 value for oxygen saturation in further calculations, such as shunt fraction, or by assuming the value obtained is equivalent to fractional oxyhemoglobin.

$$sO_2 = 100 \frac{(X^3 + 150X)}{X^3 + 150X + 23400}$$

$$\text{where } X = \boldsymbol{P}O_2 \bullet 10^{(0.48(pH-7.4)-0.0013(HCO_3-25))}$$

REAGENTS

Contents

Each i-STAT CG4+ cartridge contains a reference and ground electrode, and potentiometric and amperometric sensors for the measurement of specific analytes. It also contains a buffered aqueous calibrant solution with known concentrations of analytes and preservatives. A list of reactive ingredients relevant for the i-STAT CG4+ cartridge is indicated below:

Sensor	Reactive Ingredient	Biological Source	Minimum Quantity
pH	Hydrogen Ion (H^+)	N/A	6.66 pH

Sensor	Reactive Ingredient	Biological Source	Minimum Quantity
PCO_2	Carbon Dioxide (CO_2)	N/A	25.2 mmHg
Lactate	Lactate	N/A	1.8 mmol/L
	Lactate Oxidase	*Aerococcus viridans*	0.001 IU

Warnings and Precautions

- For *in vitro* diagnostic use.
- DO NOT REUSE—cartridges are intended for single-use only.
- Although the sample is contained within the cartridge, cartridges should be disposed of as biohazardous waste according to local, state, and national regulatory guidelines.

For additional warnings and precautions about the i-STAT System refer to the i-STAT 1 System Manual located at www.pointofcare.abbott.

Storage Conditions

- Refrigerated at 2-8°C (35-46°F) until expiration date.
- Room Temperature at 18-30°C (64-86°F). Recommended shelf life is 2 months.

INSTRUMENTS

The i-STAT CG4+ cartridge is intended for use with the i-STAT 1 analyzer.

For a detailed description of the instrument and system procedures, refer to the i-STAT 1 System Manual located at www.pointofcare.abbott.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

Arterial or venous whole blood
Sample Volume: 95 µL

Blood Collection Options and Test Timing (time from collection to cartridge fill)

Analyte	Syringes*	Test Timing	Evacuated Tubes	Test Timing
pH ***P***CO_2 ***P***O_2	With balanced heparin anticoagulant or lithium heparin anticoagulant (syringe must be filled to labeled capacity) • Maintain anaerobic conditions. • Remix thoroughly before filling cartridge.	10 minutes	With lithium heparin anticoagulant (tubes must be filled to labeled capacity) • Maintain anaerobic conditions. • Remix thoroughly before filling cartridge	10 minutes
Lactate	With balanced heparin anticoagulant or lithium heparin anticoagulant (syringe must be filled to labeled capacity) • Mix thoroughly before filling cartridge.	Immediately	With lithium heparin anticoagulant (tubes must be filled to labeled capacity) • Mix thoroughly before filling cartridge.	Immediately

* Do Not Use Heparin lock flush solution syringes

PROCEDURE FOR PATIENT TESTING

Each cartridge is sealed in a foil pouch for protection during storage--do not use if pouch has been punctured.

- A cartridge should not be removed from its protective pouch until it is at room temperature (18-30 °C or 64-86 °F). For best results, the cartridge and analyzer should be at room temperature.
- Since condensation on a cold cartridge may prevent proper contact with the analyzer, allow refrigerated cartridges to equilibrate at room temperature for 5 minutes for a single cartridge and 1 hour for an entire box before use.
- Use a cartridge immediately after removing it from its protective pouch; prolonged exposure may cause a cartridge to fail a Quality Check.
- Do not return unopened, previously refrigerated cartridges to the refrigerator.
- Cartridges may be stored at room temperature for the time frame indicated on the cartridge box.

Filling and Sealing the Cartridge (after cartridge has been equilibrated and blood sample has been collected)

1. Place the cartridge on a flat surface.
2. Mix the sample thoroughly. Invert a lithium heparin blood collection tube at least 10 times. If sample was collected into a syringe, invert syringe for 5 seconds then roll the syringe between the palms (hands parallel to the ground) for 5 seconds, flip and roll for an additional 5 seconds. The blood in the hub of the syringe will not mix, therefore expelling 2 drops before filling a cartridge is desired. Note that it may be difficult to properly mix a sample in a 1.0 mL syringe.
3. Fill the cartridge immediately after mixing. Direct the hub of syringe or tip of the transfer device (pipette or dispensing tip) into the sample well of the cartridge.
4. Slowly dispense sample into the sample well until the sample reaches the fill mark indicated on the cartridge. Cartridge is properly filled when the sample reaches the 'fill to' mark and a small amount of sample is in the sample well. The sample should be continuous, no bubbles or breaks (see System Manual for details).
5. Fold the snap closure of the cartridge over the sample well.

Performing Patient Analysis

1. Press the power button to turn on the handheld.
2. Press 2 for *i-STAT Cartridge*.
3. Follow the handheld prompts.
4. Scan the lot number on the cartridge pouch.
5. Continue normal procedures for preparing the sample, and filling and sealing the cartridge.
6. Push the sealed cartridge into the handheld port until it clicks into place. Wait for the test to complete.
7. Review the results.

For additional information for cartridge testing, refer to the i-STAT 1 System Manual located at www.pointofcare.abbott.

Analysis Time
Approx. 130–200 seconds

Quality Control

The i-STAT quality control regimen comprises four aspects, with a system design that reduces the opportunity for error, including:

1. A series of automated, on-line quality measurements that monitors the sensors, fluidics, and instrumentation each time a test is performed.
2. A series of automated, on-line procedural checks that monitor the user each time a test is performed.

3. Liquid materials that are used to verify the performance of a batch of cartridges when they are first received or when storage conditions are in question. The performance of this procedure is not a manufacturer's system instruction.
4. Traditional quality control measurements that verify the instrumentation using an independent device, which simulates the characteristics of the electrochemical sensors in a way that stresses the performance characteristics of the instrumentation.

For additional information on Quality Control, refer to the i-STAT 1 System Manual located at www.pointofcare.abbott.

Calibration Verification

Calibration Verification is a procedure intended to verify the accuracy of results over the entire measurement range of a test. The performance of this procedure is not a manufacturer's system instruction. However, it may be required by regulatory or accreditation bodies. While the Calibration Verification Set contains five levels, verification of the measurement range could be accomplished using the lowest, highest and mid-levels.

For additional information on Calibration Verification, refer to the i-STAT 1 System Manual located at www.pointofcare.abbott.

EXPECTED VALUES

TEST	UNITS *	REPORTABLE RANGE†	REFERENCE RANGE *(arterial)*	REFERENCE RANGE *(venous)*
MEASURED				
pH	pH units	7.00 - 7.70	7.35 - 7.45 [13]	7.31 – 7.41**
PO_2	mmHg	15 – 530	80 – 105 [14***]	
	kPa	2.0 – 70.6	10.7 - 14.0 [14***]	
PCO_2	mmHg	15 - 130	35 - 45 [13]	41 - 51
	kPa	2.00 –17.33	4.67 - 6.00	5.47 - 6.80
Lactate/Lac	mmol/L	0.30 - 20.00	0.36 - 1.25 [2****]	0.90 - 1.70 [2****]
	mg/dL	2.7 – 180.2	3.2 - 11.3 [2****]	8.1 - 15.3 [2****]
CALCULATED				
Bicarbonate/ HCO_3	mmol/L (mEq/L)	1.0 – 85.0	22 – 26**	23 – 28**
TCO_2	mmol/L (mEq/L)	5 - 50	23 – 27**	24 – 29**
Base Excess/ BE	mmol/L (mEq/L)	(-30) – (+30)	(-2) – (+3) [13]	(-2) – (+3) [13]
sO_2	%	0 - 100	95 – 98 [14]	

***** The i-STAT System can be configured with the preferred units. Not applicable for pH test.

****** Calculated from Siggard-Andersen nomogram [1].

******* The reference ranges shown are for a healthy population. Interpretation of blood gas measurements depend on the underlying condition (e.g., patient temperature, ventilation, posture and circulatory status).

******** The i-STAT reference ranges for whole blood listed above are similar to reference ranges derived from serum or plasma measurements with standard laboratory methods.

† Incorrect Action / Reference range settings for pH, ***P***O_2, or ***P***CO_2 may result in CG4+ cartridge testing being blocked. Verify that instrument and customization settings support running the cartridge prior to use. See i-STAT/DE Customizing Reference & Action Ranges, Art 770546-00 for instructions.

Unit Conversion

- ***P*O₂ and *P*CO₂:** To convert ***P***O_2 and ***P***CO_2 results from mmHg to kPa, multiple the mmHg value by 0.133.

- **Lactate/Lac:** To convert a lactate result from mmol/L to mg/dL, multiply the mmol/L value by 9.01.

The reference ranges programmed into the analyzer and shown above are intended to be used as guides for the interpretation of results. Since reference ranges may vary with demographic factors such as age, sex and heritage, it is recommended that reference ranges be determined for the population being tested.

METROLOGICAL TRACEABILITY

The measured analytes in the i-STAT CG4+ cartridge tests are traceable to the following reference materials or methods. The i-STAT controls and calibration verification materials are validated for use only with the i-STAT System and assigned values may not be commutable with other methods.

pH

The i-STAT System test for pH measures the hydrogen ion amount-of-substance concentration in the plasma fraction of arterial or venous whole blood (expressed as the negative logarithm of the relative molal hydrogen ion activity) for *in vitro* diagnostic use. pH values assigned to the i-STAT System controls and calibration verification materials are traceable to the U.S. National Institute of Standards and Technology (NIST) standard reference materials SRMs 186-I, 186-II, 185, and 187.

PO_2

The i‑STAT System test for oxygen partial pressure measures oxygen partial pressure in arterial or venous whole blood (unit kPa) for *in vitro* diagnostic use. PO_2 values assigned to the i‑STAT System controls and calibration verification materials are traceable to U.S. National Institute of Standards and Technology (NIST) standard reference materials via commercially available certified specialty medical gas standards.

PCO_2

The i‑STAT System test for carbon dioxide partial pressure measures carbon dioxide partial pressure in arterial or venous whole blood (unit kPa) for *in vitro* diagnostic use. PCO_2 values assigned to the i‑STAT System controls and calibration verification materials are traceable to U.S. National Institute of Standards and Technology (NIST) standard reference materials via commercially available certified specialty medical gas standards.

Lactate/Lac

The i-STAT System test for lactate measures L-lactate amount-of-substance concentration in the plasma fraction of arterial or venous whole blood (unit mmol L^{-1}) for *in vitro* diagnostic use. Presently, no international conventional reference measurement procedure or international conventional calibrator for lactate is available. Lactate values assigned to the i-STAT System controls and calibration verification materials are traceable to i-STAT System working calibrator prepared from sodium L-lactate (Sigma-Aldrich Fluka, >99 % purity).

Additional information regarding metrological traceability is available from Abbott Point of Care Inc.

PERFORMANCE CHARACTERISTICS

The typical performance of the i-STAT CG4+ cartridge tests with the i-STAT 1 System are shown below.

Precision

Precision data was collected in studies based on CLSI guideline EP05-A3. [15] Precision studies were performed using five levels of aqueous materials for pH, PO_2, PCO_2, and Lactate. Duplicates of each level were tested twice a day for 20 days.

The statistics for Mean, Standard Deviation (SD) and Coefficient of Variation (CV) are represented below. This is representative data; results in individual laboratories may vary.

Analyte	Units	Fluid Level	N	Mean	SD	CV (%)
pH	pH units	CV L1	80	6.5215	0.00435	0.07
		CV L2	81	7.0199	0.00287	0.04
		CV L3	80	7.4758	0.00279	0.04
		CV L4	80	7.7551	0.00241	0.03
		CV L5	80	7.9862	0.00369	0.05
PO_2	mmHg	CV L1	80	70.2	2.45	3.5
		CV L2	81	85.7	2.69	3.1
		CV L3	80	120.4	2.66	2.2
		CV L4	80	152.9	3.02	2.0
		CV L5	80	363.4	6.98	1.9
PCO_2	mmHg	CV L1	80	87.08	1.349	1.5
		CV L2	81	59.48	0.921	1.5
		CV L3	80	29.24	0.675	2.3
		CV L4	80	21.14	0.552	2.6
		CV L5	80	15.05	0.506	3.4
Lactate	mmol/L	CV L1	80	18.448	0.1655	0.9
		CV L2	80	7.967	0.0495	0.6
		CV L3	79	2.251	0.0082	0.4
		CV L4	80	0.924	0.0122	1.3
		CV L5	80	0.497	0.0133	2.7

Whole blood precision was evaluated using whole blood venous and arterial specimens collected with lithium heparin. The repeatability analysis was conducted using the data collected across multiple point of care sites. The mean values for each sample were divided into subintervals for each sample type.

Analyte	Units	Sample Type	Sample Range	N	Mean	SD	CV (%)
pH	pH units	Venous Whole Blood	<7.30	20	7.202	0.0064	0.09
			7.30 – 7.45	77	7.374	0.0060	0.08
			>7.45	7	7.585	0.0030	0.04
		Arterial Whole Blood	<7.30	22	7.259	0.0059	0.08
			7.30 – 7.45	119	7.389	0.0060	0.08
			>7.45	36	7.494	0.0047	0.06
PO_2	mmHg	Venous Whole Blood	<50	59	28.8	0.9	3.0
			50 - 100	27	58.2	2.0	3.4
			100 - 250	4	188.6	1.4	0.7
			>250	6	450.0	12.4	2.8
		Arterial Whole Blood	<50	2	40.3	0.5	1.2
			50 - 100	65	77.5	3.4	4.4
			100 - 250	78	156.6	3.7	2.4
			>250	33	355.6	8.5	2.4
PCO_2	mmHg	Venous Whole Blood	<35	6	16.83	0.29	1.7
			35 - 62.5	83	46.23	0.77	1.7
			>62.5	26	91.61	0.73	0.8
		Arterial Whole Blood	<35	33	31.23	0.51	1.6
			35 - 62.5	140	42.65	0.90	2.1
			>62.5	4	74.36	0.37	0.5
Lactate	mmol/L	Venous Whole Blood	<1.0	50	0.70	0.016	2.26
			1.0 – 5.0	62	1.83	0.021	1.14
			>5.0	11	12.88	0.200	1.55
		Arterial Whole Blood	<1.0	57	0.72	0.018	2.49
			1.0 – 5.0	42	1.87	0.020	1.08
			>5.0	8	8.55	0.036	0.42

Method Comparison

Method comparison was demonstrated in a study based on CLSI guideline EP09cED3. [16]

Lithium heparin venous and arterial whole blood specimens collected across multiple point of care sites were evaluated and analyzed in singlicate on the i STAT 1 analyzer against the comparative method. For pH, ***P***O_2, and ***P***CO_2, a Passing Bablok linear regression analysis was performed using the first replicate result from the i-STAT 1 versus the singlicate result of the comparative method. For lactate, the first replicate result from the i-STAT 1 was compared to the mean result of the comparative method.

In the method comparison table, N is the number of specimens in the data set, and r is the correlation coefficient.

Method comparison results comparing the i-STAT pH, ***P***O_2, ***P***CO_2, and Lactate performance on the i-STAT 1 to comparative methods are shown in the table below.

Analyte	Comparative Method	N	Slope	Intercept	r	Xmin	Xmax
pH	Radiometer ABL800 FLEX blood gas analyzer	316	1.05	-0.34	0.97	7.001	7.661
PO_2	Radiometer ABL800 FLEX blood gas analyzer	308	1.03	-3.96	0.99	15.4	480.0
PCO_2	Radiometer ABL800 FLEX blood gas analyzer	327	1.01	-1.29	0.99	15.1	128.0
Lactate	epoc® Blood Analysis System	246	0.96	0.08	1.00	0.320	19.980

Linearity

Linearity studies were performed based on guidance from CLSI EP06-A [17]. The results using lithium heparin whole blood samples demonstrated linearity across the reportable range of the analytes described in the "Expected Values" section above.

LIMITATIONS OF THE PROCEDURE

The analyte results should be assessed in conjunction with the patient's medical history, clinical examination, and other findings. If results appear inconsistent with the clinical assessment, the patient sample should be retested using another cartridge.

Interference Testing

Interference studies were based on CLSI guideline EP07 3rd edition [18]. The substances listed were evaluated in lithium heparin whole blood for relevant analytes. For those identified as an interferant the interference is described.

Substance*	Test Concentration mmol/L	Test Concentration mg/dL	Analyte	Interference (Yes/No)	Comment
Acetaldehyde [a]	45 µmol/L [19]	0.2	Lactate	No	
Acetaminophen	1.03	15.6	pH	No	
			PO_2	No	
			PCO_2	No	
			Lactate	No	
Ascorbic Acid	0.298	5.25	Lactate	No	
Atracurium [a]	0.0287	3.57	pH	No	
			PO_2	No	
			PCO_2	No	
Bilirubin	0.684	40	pH	No	
			PO_2	No	
			PCO_2	No	
			Lactate	No	
Bromide [a] (lithium bromide)	40.7 [20 21 22]	325.7	Lactate	Yes	Decreased results ≥ 40.7 mmol/L
β-Hydroxybutyric Acid [a]	6 [23]	62	Lactate	No	
Calcium (calcium chloride)	5	20	pH	No	

Substance*	Test Concentration		Analyte	Interference (Yes/No)	Comment
	mmol/L	mg/dL			
			PO_2	No	
			PCO_2	No	
Dopamine (dopamine hydrochloride)	4.06 µmol/L	0.0621	Lactate	No	
Ethanol	130	600	pH	No	
			PO_2	No	
			PCO_2	No	
Formaldehyde [a]	0.133 [19]	0.399	Lactate	No	
Glycolic Acid [a]	10.0 [19]	76.1	Lactate	Yes	Increased results ≥ 1.18 mmol/L
Hemoglobin	10 g/L	1000	pH	No	
			PO_2	No	
			PCO_2	No	
			Lactate	No	
Hydroxyurea	0.405	3.08	Lactate	No	
Ibuprofen	1.06	21.9	pH	No	
			PO_2	No	
			PCO_2	No	
Intralipid (Intralipid 20%)	N/A	2493	pH	No	
			PO_2	No	
			PCO_2	No	
		3423	Lactate	No	
Morphine	0.0273	0.78	pH	No	
			PO_2	No	
			PCO_2	No	
N-Acetyl-Cysteine	0.92	15	Lactate	No	
Potassium (potassium chloride)	8	59.6	pH	No	
			PO_2	No	
			PCO_2	No	
Pyruvate (lithium pyruvate)	0.57	5	Lactate	No	
Salicylate (lithium salicylate)	0.207	2.86	Lactate	No	
Sodium (sodium chloride)	170	993.48	pH	No	
			PO_2	No	
			PCO_2	No	
Thiocyanate (lithium thiocyanate)	0.898	5.22	Lactate	No	
Thiopental	1660	40.2	pH	No	
			PO_2	No	
			PCO_2	No	
Triglyceride	16.94	1500	pH	No	
			PO_2	No	
			PCO_2	No	
			Lactate	No	
Uric Acid	1.4	23.5	Lactate	No	

[a] The test concentration for this substance is not included in CLSI guideline EP37 1st edition. [24]
*The compound tested to evaluate the interfering substance is presented in parenthesis.

This is representative data and results may vary from study to study due to matrix effects. Viscosity, surface tension, turbidity, ionic strength and pH are common causes of matrix effects. It is possible that interfering substances other than those tested may be encountered. The degree of interference at concentrations other than those listed might not be predictable.

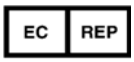
- Relevant comments regarding interference of Bromide and Glycolic acid are noted below:
    - Bromide at 2.5 mmol/L is the peak plasma concentration associated with halothane anesthesia, in which bromide is released.
    - Glycolyic acid is a product of ethylene glycol metabolism. Glycolic acid at a concentration of 10.0 mmol/L can cause increased i-STAT Lactate results. At this level another method should be used to measure lactate. Unexpected increased lactate concentrations caused by glycolic acid may be a clue to the possibility of ethylene glycol ingestion as the cause of an otherwise

unknown high anion gap metabolic acidosis [25] [26]. In a study of 35 patients who had ingested ethylene glycol, initial glycolic acid concentrations of 0 to 38 mmol/L corresponded to ethylene glycol levels of 0.97 – 130.6 mmol/L. [26]

Factors Affecting Results

Factor	Analyte	Effect
Exposing the sample to air	$\boldsymbol{P}O_2$	Exposure of the sample to air will cause an increase in $\boldsymbol{P}O_2$ when values are below 150 mmHg and a decrease in $\boldsymbol{P}O_2$ when values are above 150 mmHg (approximate $\boldsymbol{P}O_2$ of room air).
	pH	Exposing the sample to air allows CO_2 to escape which causes $\boldsymbol{P}CO_2$ to decrease and pH to increase and HCO_3 and TCO_2 to be under-estimated.
	$\boldsymbol{P}CO_2$	
	HCO_3	
	TCO_2	
Venous stasis	pH	Venous stasis (prolonged tourniquet application) and forearm exercise may decrease pH due to localized production of lactic acid.
Hemodilution	pH	Hemodilution of the plasma by more than 20% associated with priming cardiopulmonary bypass pumps, plasma volume expansion or other fluid administration therapies using certain solutions may cause clinically significant error on sodium, chloride, ionized calcium and pH results. These errors are associated with solutions that do not match the ionic characteristics of plasma. To minimize these errors when hemodiluting by more than 20%, use physiologically balanced multi-electrolyte solutions containing low-mobility anions (e.g., gluconate).
Cold temperature	$\boldsymbol{P}O_2$	Do not ice samples before testing - $\boldsymbol{P}O_2$ results may be falsely elevated in cold samples. Do not use a cold cartridge - $\boldsymbol{P}O_2$ results may be falsely decreased if the cartridge is cold.
Sample collection	Lactate	Special collection procedures are necessary to prevent changes in lactate both during and after the blood is drawn. For steady state lactate concentrations, patients should be at rest for 2 hours and fasting. Venous samples should be obtained without the use of a tourniquet or immediately after the tourniquet is applied. Both venous and arterial samples may be collected into heparinized syringes.
Allowing blood to stand (without exposure to air)	pH	pH decreases on standing anaerobically at room temperature at a rate of 0.03 pH units per hour. [1]
	$\boldsymbol{P}O_2$	Standing anaerobically at room temperature will decrease $\boldsymbol{P}O_2$ at a rate of 2–6 mmHg per hour. [1]
	$\boldsymbol{P}CO_2$	Standing anaerobically at room temperature will increase $\boldsymbol{P}CO_2$ by approximately 4 mmHg per hour.[1]
	HCO_3	Allowing blood to stand (without exposure to air) before testing allows $\boldsymbol{P}CO_2$ to increase and pH to decrease, which will cause HCO_3 and TCO_2 to be over-estimated, due to metabolic processes.[1]
	TCO_2	
	Lactate	Samples for lactate should be analyzed immediately on drawing as lactate increases by as much as 70% within 30 minutes at 25 ºC as a result of glycolysis. [2]
Underfilled or partial draw tubes	$\boldsymbol{P}CO_2$	The use of partial draw tubes (evacuated tubes that are adjusted to draw less than the tube volume, e.g., a 5 mL tube with enough vacuum to draw only 3 mL) is not recommended due to the potential for decreased $\boldsymbol{P}CO_2$, HCO_3 and TCO_2 values. Underfilling blood collection tubes may also cause decreased $\boldsymbol{P}CO_2$, HCO_3 and TCO_2 results. Care must be taken to eliminate "bubbling" of the sample with a pipette when filling a cartridge to avoid the loss of CO_2 in the blood.
	HCO_3	
	TCO_2	
Method of calculation	sO_2	Calculated sO_2 values from a measured PO_2 and an assumed oxyhemoglobin dissociation curve may differ significantly from the direct measurement [12].
$\boldsymbol{P}O_2$ sensitivity	$\boldsymbol{P}CO_2$	In patient samples where the $\boldsymbol{P}O_2$ is > 100 mmHg above the normal range (80-105 mmHg), an increase in $\boldsymbol{P}CO_2$ of approximately 1.5 mmHg (with a range of 0.9 to 2.0 mmHg) may be observed for every 100 mmHg increase in $\boldsymbol{P}O_2$. For example, if an oxygenated patient has a measured $\boldsymbol{P}O_2$ of 200 mmHg, and a normal $\boldsymbol{P}O_2$ is 100 mmHg, the impact to the $\boldsymbol{P}CO_2$ result may be increased by approximately 1.5 mmHg.

KEY TO SYMBOLS

Symbol	Definition/Use
	2 months room temperature storage at 18-30^{0}C
	Use by or expiration date. An expiration date expressed as YYYY-MM-DD means the last day the product can be used.
	Manufacturer's lot number or batch code. The lot number or batch will appear adjacent to this symbol.
	Sufficient for <n> tests
	Authorized representative for Regulatory Affairs in the European Community.
	Temperature limitations. The upper and lower limits for storage are adjacent to upper and lower arms.
	Catalog number, list number, or reference
	Do not reuse.
	Manufacturer
	Consult instructions for use or see System Manual for instructions.
	*In vitro* diagnostic medical device
	Compliance to the European directive on *in vitro* diagnostic devices (98/79/EC)
	For prescription use only.

Additional Information: To obtain additional product information and technical support, refer to the company website at www.pointofcare.abbott.

REFERENCES

1 E.L. Pruden, O. Siggard-Andersen, and N.W. Tietz, Blood Gases and pH, in Tietz Textbook of Clinical Chemistry, Second Edition, ed. C.A. Burtis and E.R. Ashwood. (Philadelphia: W.B. Saunders Company, 1994).

2 D.B. Sacks, Carbohydrates, in Tietz Textbook of Clinical Chemistry, Second Edition, ed. C.A. Burtis and E.R. Ashwood, (Philadelphia: W.B. Saunders Company, 1994).

3 Jones AE, Puskarich MA. Sepsis-induced tissue hypoperfusion. Crit Care Clin. 2009;25:769-779.

4 Dellinger RP, Levy MM, Carlet JM, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. Crit Care Med. 2008;36:296-327.

5 Shapiro NI, Fisher C, Donnino M, et al. The feasibility and accuracy of point-of-care lactate measurement in emergency department patients with suspected infection. J Emerg Med. 2010;39:89-94.

6 Crowl AC, Young JS, Kahler DM, et al. Occult hypoperfusion is associated with increased morbidity in patients undergoing early femur fracture fixation. J Trauma. 2000;48:260-267.

7 Paladino L, Sinert R, Wallace D, et al. The utility of base deficit and arterial lactate in differentiating major from minor injury in trauma patients with normal vital signs. Resuscitation. 2008;77:363-368.

8 Blow O, Magliore L, Claridge JA, et al. The golden hour and the silver day: detection and correction of occult hypoperfusion within 24 hours improves outcome from major trauma. J Trauma. 1999;47:964-969.

9 Bakker J and Pinto de Lima A. Increased blood lacate levels: an important warning signal in surgical practice. Crit Care. 2004;8:96-98.

10 Husain FA, Martin MJ, Mullenix PS, et al. Serum lactate and base deficit as predictors of mortality and morbidity. Am J Surg. 2003;185:485-491.

11 Rossi AF, Khan DM, Hannan R, et al. Goal-directed medical therapy and point-of-care testing improve outcomes after congenital heart surgery. Intensive Care Med. 2005;31:98-104.

12 CLSI. Blood Gas and pH Analysis and Related Measurements; Approved Guideline. CLSI document C46-A [ISBN 1-56238-444-9]. CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898, USA 2001.

13 P.C. Painter, J.Y. Cope, J.L. Smith, “Reference Ranges, Table 41–20” in Tietz Textbook of Clinical Chemistry - Second Edition, C.A. Burtis and E.R. Ashwood, eds. (Philadelphia: W.B. Saunders Company, 1994).

14 B.E. Statland, Clinical Decision Levels for Lab Tests (Oradell, NJ: Medical Economics Books, 1987).

15 CLSI. Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline - Third Edition. CLSI document EP05-A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2014.

16 Clinical and Laboratory Standards Institute (CLSI). Measurement Procedure Comparison and Bias Estimation Using Patient Samples – Third Edition. CLSI document EP09c ED3. Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania, 19087, USA, June 2018.

17 CLSI. Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline – Third Edition. NCCLS document EP06-A [ISBN 1-56238-498-8]. Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087, USA 2003.

18 Clinical and Laboratory Standards Institute (CLSI). Interference Testing in Clinical Chemistry – Third Edition. CLSI guideline EP07. Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087, USA; 2018.

19 Wu, Alan H.B. Tietz Clinical Guide to Laboratory Tests (Fourth Edition). W. B. Saunders Elsevier (2006).

20 Kharasch E.D, Hankins D., Mautz D., Thummel K.E. Identification of the enzyme responsible for oxidative halothane metabolism: implications for prevention of halothane hepatitis. Lancet 1996; 347:1367-71.

21 Morrison J.E., Friesen R.H., Elevated serum bromide concentrations following repeated halothane anaesthesia in a child. Can J Asaesth 1990; 37 (7): 801-803.

22 Hankins D.C, Kharasch E.D., Determination of the halothane metabolites trifluoroacetic acid and bromide in plasma and urine by ion chromatography. J of Chromatography B. 692 (1997) 413-418.

23 Charles R.A, Bee Y.M, Eng P.H.K., Goh S.Y. Point of care blood ketone testing: screening for diabetic ketoacidosis at the emergency department. Singapore Med J 2007; 48 (11): 986.

24 Clinical and Laboratory Standards Institute (CLSI). Supplemental Tables for Interference Testing

in Clinical Chemistry - First Edition. CLSI supplement EP37. Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087, USA; 2018.
25 Morgan, TJ, Clark C, Clague A. Artifactual elevation of measured plasma L-lactate concentration in the presence of glycolate. Crit Care Med 1999; 27:2177-2179.
26 Porter WH, Crellin M, Rutter PW, Oeltgen P. Interference by Glycolic Acid in the Beckman Synchron Method for Lactate: A Useful Clue for Unsuspected Ethylene Glycol Intoxication. Clin Chem 2000; 46:874-875.